Comment on


“Metformin use and lung cancer risk –Letter.”

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To the Editor: Here, Sakoda et al. reported that there is no affect of metformin, a cancer chemopreventive agent candidate, on overall lung cancer risk, but in subgroup analysis, metformin use showed higher small cell carcinoma risk, although not statistically significant. We are very impressed by this data because we also experienced modifier effects of smoking in our cancer prevention trials. In addition, several human trials demonstrate that there is an inverse association between non-smokers and smokers in the cancer preventive effects using cancer chemopreventive agents, such as
beta-carotene, and tea polyphenols. Carotene and Retinol Efficacy Trial (CARET) and Alpha-Tocopherol Beta Carotene Cancer Prevention Study (ATBC Study) indicated that lung cancer incidence was increased among smokers who received beta-carotene (1, 2). Tea polyphenol affects gastric cancer risk according to smoking status, although there is a consistent association between smoking and gastric cancer (3). We recently performed two double-blind, randomized studies using aspirin, in which aspirin similarly increased the risk of colorectal adenomas in the smokers. One is the J-FAPP Study II that included 34 subjects with familial adenomatous polyposis, and compared the effects of aspirin enteric-coated tablets (100 mg/day) and a placebo, with an intervention period of 6 to 10 months (4). The other is the J-CAPP Study that included 311 subjects with prior colorectal tumors (adenomas or early-stage adenocarcinomas), using the same aspirin enteric-coated tablets and placebo for 2 years (5). In the J-FAPP Study II, the odds ratio (OR) for a reduction in the diameter of polyps was 0.10 (CI, 0.01-0.98) in non-smokers (never-smokers/ex-smokers) comparing the aspirin group vs the placebo group, and 3.00 (CI, 0.15-59.89) in current smokers. In the J-CAPP Study, the OR for the presence or absence of tumor recurrence was 0.37 (CI, 0.21-0.68) in non-smokers and 3.45 (CI, 1.12-10.64) in current smokers. The mechanism by which smoking influences the effect of aspirin is unknown. Further studies are warranted to determine if consistent results are obtained by smoking status plus use of cancer chemopreventive agents because this issue is very important for clinical use of cancer chemopreventive agents in the future.


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